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ARTERIOSCLEROSIS IN ITS RELATION TO DISEASES OF THE NERVOUS SYSTEM.

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CLINICAL ASPECT. BY EDWARD D. FISHER, M.D.

The changes in the arteries, as far as the pathological condition can be demonstrated, show that arteritis or arteriosclerosis, whether due to infection or so-called senile changes is the same in character, at least in the later stages. Still the clinical picture is so different, as a rule, that one is forced to come to the conclusion that later studies under improved methods must demonstrate that we have to do with distinct lesions, at least in the early stages, whatever the end results may be.

Even from what has been demonstrated we can assume that syphilis has a tendency to cause a periarteritis, involving, perhaps, the adventitia or external coat primarily, and leading later to great thickening of all the coats, which thus occludes the lumen of the vessels, causing thrombosis.

While, indeed, we observe clinically that cerebral hemorrhage occurs in syphilitic endarteritis, it is far less frequent than thrombosis. Atheroma, on the other hand, usually primarily involves the intima, ultimately affecting the other coats, and, by subsequent degeneration, forms patches of calcification which may be continuous in the long axis of the vessels, without marked thickening of the coats of the vessels.

This arteriosclerosis is very general, involving the smaller arteries and leading to hemorrhage through small miliary aneurisms of the small straight arteries in the brain.

Studying the various diseases of the nervous system as resulting from arteriosclerosis, whether atheromatous in type or of syphilitic origin, the most frequently observed are apoplexy, whether due to occlusion of the vessels or hemorrhage; general paralysis of the insane; multiple sclerosis; cerebral atrophy, and cerebral syphilis, which must be recognized as a distinct entity.

We will first consider cerebral apoplexy, the one most frequently observed. One finds that hemorrhage into the brain is most common after forty, while it may occur in children following the infectious disease in which an arteritis (acute) is present; or, again, cases of marasmus have been reported, with definite pathological changes, as advanced arteriosclerosis, probably chronic in its course. The usual clinical picture, however, in the first class of adult cases of hemorrhage, is marked arterial degeneration as demonstrated during life by the hard, thickened vessels observed especially in the radial and temporal arteries, and which can be observed also in the retinal vessels, and while not clinically demonstrable is also present, as shown by Broadbent, in the aorta. There is usually high arterial tension and the arteries are incompressible. We early have cardiac hypertrophy, which later passes on to dilatation; associated with this there is often evidence of interstitial nephritis, as shown by low specific gravity of the urine; intermittent or constant albuminuria and casts; and not infrequently the ophthalmoscope demonstrates retinal hemorrhage. The only etiological factors we may find in these cases may be overwork or strain—physical or mental; overeating; moderate or excessive use of alcohol; gouty, or less often rheumatic diathesis; or heredity.

The course of a case such as this may be short or protracted, frequently modified by change in the method of living or medicine. It is impossible in these cases to state whether the nephritis is an important factor in causing the disease. No doubt in some it is, the defective elimination of the toxins by the kidneys causing the high tension in the arteries, and acting especially in causing the arteritis of the small peripheral vessels, by which they lose their elasticity and offer much resistance to the course of the blood, then, again, secondarily calling upon the heart for extra exertion and causing its hypertrophy as well as hypertrophy of the muscular coats of the vessels themselves, the larger as well as the smaller, for we must not forget that in the circulation we have two important elements in its propulsion, the heart itself and the muscular elements of the arteries, sometimes called "the second heart."

However, while we must recognize nephritis as a cause of arteriosclerosis, still, as Broadbent has said, many cases are due to a primary arteriosclerosis, which has involved the arteries of the whole body, including the kidneys, so that we find disease of the cerebral vessels, of the aorta, of the coronary arteries, the vasa vasorum of the arteries themselves, and of the various organs, kidneys, liver, and the peripheral arteries.

Another class of cases, however, which also result in hemorrhage, do not present the evidence of high tension or thickening in the walls of the vessels; in fact, post mortem the arteries at the base appear thin and soft. In these cases, however, the arterioles are found diseased in the region of the internal capsules, and liable to rupture.

Perhaps at this time it would be well to refer to the cases of cerebral hemorrhage occurring in typhoid fever, scarlet fever, and the other infectious diseases, or, again, in rabies and in the puerperal period. We are dealing here with probably an acute arteritis as shown in the case of rabies related by Dr. Brooks, with the added change in the condition of the blood which renders the blood less capable of being transmitted through the blood vessels. Here we commonly have hemorrhage, or less frequently thrombosis. The latter condition of thrombosis was seen in a young woman, aged twenty-two, a primipara, who, in the third week after confinement, had hemiplegia in the right side, associated with which was the usual mental disturbance found in puerperal mania. As the patient completely recovered from the paralysis and aphasia, although not demonstrable by autopsy, I can only consider that we were dealing with a thrombosis due to blood changes, which was ultimately carried away in the circulation or absorbed.

Different, indeed, is the condition of syphilitic hemiplegia. In a typical case occurring in early life, usually six to ten years after the primary lesion of syphilis, there is no evidence of high pulse tension, no cardiac hypertrophy or nephritis, the peripheral arteries show no signs of hard, resisting walls. While the onset may be that of a hemorrhage, the usual condition is due to thrombosis. The onset is usually slow; the patient may, indeed, at no time lose consciousness, and may be able to fully describe the course of the onset and the subsequent complete hemiplegia and aphasia.

The commonest situation of cerebral hemorrhage is in the region of the internal capsule. While we find the arteries at the base of the brain in the circle of Willis the seat of atheromatous changes, as well as the basilar artery, they rarely are the seat of hemorrhage. The reason why the smaller internal vessels are usually affected is that they enter the brain perpendicularly, are straight in their course, and do not anastomose. In atheroma of the vessels involving the large arteries, there is no interruption to the full impact of the blood and no distribution as in the circle of Willis, and their diseased walls soon give way.

Thrombosis and aneurism, on the other hand, are most commonly found in the pons and at the base.

Apart from the disease just considered, perhaps the most usual cerebral disease is general paresis, or dementia paralytica. This is essentially a vascular disease, and in the majority, if not in all cases, due to syphilitic endarteritis, if we can use such a term, which, as I have previously said, recent pathology seems to deny.

Adolf Meyer, in a recent communication in regard to the arterial changes found in general paresis, says that there is nothing to distinguish them from the usual form of arterial disease in which there is no mental disturbance. Arteriosclerosis of the heart and the aorta, and nephritis, are often found in the insane; but it is not often that insanity can be directly referred to them.

In general paresis we find a chronic progressive meningoencephalitis, associated with cranial nerve lesion and degeneration in the spinal cord tracts, either of the posterior columns or lateral motor tracts, dependent on arteriosclerosis.

We are evidently not dealing with a direct syphilitic infiltration in this disease, but the tendency to arteriofibrosis which syphilis impresses on the system as a whole. The same can be said of tabes. We do not find the vessels the seat of gummatous infiltration, as in cerebro-spinal syphilis, but, rather, subject to changes characterized by general thickening of the walls, thus interfering with the general nutrition.

While some writers have drawn a very close analogy between general paresis and tabes, reporting cases of the latter passing into general paresis, I have rarely observed a typical case of tabes become paretic. We have in both diseases the Argyll-Robertson pupil peculiar to both of these diseases, and these only; but a patient with marked ataxia, diplopia, optic atrophy, lightning pain, etc., may thus continue for years without change or even with an improvement in his symptoms without at any time showing the slightest mental disturbance.

Few cases of general paresis occur without evidence of some spinal involvement, and especially in the class of atypical cases which last for seven or eight years. Here there is often marked sclerosis of the motor tracts of the cord, or, again, of the posterior tracts. Post mortem we usually find degeneration in both tracts, but rarely so definitely confined to one system tract as in tabes. On the other hand, in old cases of tabes, it is not unusual to find the lateral tracts also to some degree affected.

While in tabes we cannot hope for a cure, all such reported cases being to my mind cases of mistaken diagnosis, being either spinal syphilis or multiple neuritis, still much can be done to alleviate symptoms. The ataxia, by re-educating the muscle, can be reduced; and, again, one must not forget that the disease itself often comes to a standstill, either permanently or for a time. I encourage all tabetics to do anything they have the power or strength to do, especially as no mental or physical exercise can at all injure them or hasten the course of the disease.

Multiple sclerosis is due to arteriosclerosis. It is a comparatively rare disease, occurring in about one in two hundred cases in thirty-five thousand patients, presenting themselves at a clinic for nervous diseases.

There is much difference of opinion as to whether syphilitic endarteritis, to still use that term, is ever present.

The pathological changes observed in the vessels are increase in the volume or thickness of the intima, with narrowing of the lumen, or, indeed, obliteration, although this is not always found.

It is thus an inflammatory disease commencing in the blood vessels. One finds also the lymph tracts affected, and dilatation of the perivascular lymph spaces.

Erb, Gowers, Strümpell, Oppenheim and Rumpf do not consider syphilis as a factor in the disease, while Westphal and Fournier are less positive. Leyden and Goldscheider have written of the difficulty at times of differential diagnosis between spinal syphilis and sclerosis (multiple).

Buchholz reports a case which falls under the head of multiple sclerosis. In the necropsy, however, there were many syphilitic evidences; i.e., of the testicles, gumma of the temporal lobe, and specific disease of the vessels and of the pia mater. Bechterew called his case syphilitic disseminated cerebrospinal sclerosis. Schulze's case partly resembled general paresis and was distinctly specific. Rosenfeld wrote an article on endarteritis and multiple sclerosis (*Archiv für Psychiatrie und Nervenkrankheiten,* Vol. 38, No. 2, 1904). His case was typical in its clinical history. The necropsy showed the usual sclerosed spots in the brain, pons and cord; the axis cylinders persisted at least in part; some vessels showed hyaline degeneration without occlusion. The basal arteries showed disease of the intima and adventitia. In some arteries occlusion was present.

The writer does not say, however, that this is characteristic of syphilitic changes, nor does he give what is the differential characteristic.

Arteriosclerosis may be the cause of diffuse inflammation of the spinal cord; or, rather, we may define it as a combined disease of the various tracts, giving, therefore, symptoms resembling tabes and spastic paralysis. We find in the cord, as in the brain, arteriosclerosis, atheroma of the vessels, hemorrhage and thrombosis. This accounts for irregular cases of paralysis occurring in the old.

Syphilis of the brain characterizes itself by headache, mental dulness, tendency to coma, cranial nerve paralyses as seen in diplopia, ptosis, irregularity of the pupils with slowness of reaction, often transient or permanent paralysis; and, again, mental disturbances of excitement and peculiarity of speech or utterance which at times make a differential diagnosis from general paresis very difficult.

This applies also to spinal syphilis when the lesion may be so situated as to involve the posterior columns and give many if not all the symptoms of tabes. The diagnosis can be made, however, by the rapidity of the onset of the symptoms, which is rare in tabes, and also by their rapid disappearance.

We are dealing in these cases with a gummatous infiltration and not a true arteriosclerosis, which is capable of absorption under specific treatment.

Arteriosclerosis seems to me to be the basis of angina pectoris. While all our autopsies do not show disease of the coronary arteries, still general disease of the arterial system is often present in these cases. Syphilis cannot be excluded as a causative factor here.

In all cases of arteriosclerosis we must look to the predisposing cause. The kidney and heart should be carefully examined, and any deficiency of action compensated for. Overwork, overeating, sedentary habits, and the use of alcohol in excess must be modified. If a specific history, large doses of the iodides, especially in the early stages of the disease are required.

Again, I have found, when the pulse is of high tension, that thyroid extract, as, from its physiological action, one might expect, is beneficial.

In some old cases of atheroma I advise small doses of the iodide of potassium; i.e., five to ten grains, and thyroid extract, five grains, two to three times a day.

We must not forget that many of our syphilitic cases have other changes in the arteries also, due to alcoholic excesses or overwork, etc., and we may have in them also high arterial tension, nephritis and cardiac hypertrophy. In these cases much relief is obtained from continued dosage of digitalis and nitro-glycerine combined, in conjunction with some form of iron, either Blaud's pills or the newer combinations, as ovoferrin, etc. In these cases the old calomel purge once a week is not to be forgotten. I usually advise it in small doses, either one grain, or one-tenth frequently repeated. A drug also which is variously estimated as to its value, which I have long used is the proto-iodide of mercury in 1-6 grain doses, t.i.d., and this I use whether the case is syphilitic or not.

Brunton advises, for high blood pressure,

Potassium bicarbonate	grs. XXVIII
Potassium nitrate	grs. XVIII
Sodium nitrite	grs. IVss

in a glass of water in the morning.

Traumek's saline solution (inorganic serum) hypodermic,

Sodium sulphate	grms. 14
Sodium chloride	grms. 4.9
Sodium phosphate	grms. 15
Sodium carbonate	grms. 21
Potassium sulphate	grms. 40
Aq. Dist. ad	grms. 100

Dose, 1 c.c. every four to seven days.

—*Med. Press*, Nov. 26, 1903.

SUMMARY OF THE PATHOLOGY OF CEREBRO-SPINAL ARTERIOSCLEROSIS. BY HARLOW BROOKS, M.D.

Arteriosclerosis of the brain and spinal cord is occasionally found as a purely local disease and it may even be seen alone in either the brain or cord. It is, however, usually found associated with more or less general arterial disease, as a local manifestation more pronounced in the cerebrospinal tissues than elsewhere. There are reasons why this is so frequently the case, but in considering them we must also recall that the brain and cord are not alone in this peculiarity since a local arteriosclerosis of the kidney, of the pancreas and of any of the other special viscera is by no means infrequent.

Coplin finds, according to his statistics, that the cerebral arteries are more prone to arteriosclerosis than those of any other viscera, placing them as fourth in the frequency of involvement. (1, arch of aorta, 2, thoracic and abdominal aorta, 3, iliac arteries, 4, cerebral arteries.)

The reasons for this preponderance of local arteriosclerosis are variously stated. It is not due to any inherent structural peculiarities in the arteries themselves though the relation of the trunks to the surrounding tissues, and the nature of these is an important factor. Thus in the brain and cord the vessels are not united, as in most other parts of the body, directly to firm and resistant tissues, but are, in large part suspended in channels, the perivascular lymph spaces, which are crossed over by but a fragile frame-work of connective tissue and this joins the vessels to the soft, semi-gelatinous nervous pulp. This arrangement renders the vessels particularly susceptible to the mechanical factors productive of cerebro-spinal arteriosclerosis. Added to these peculiarities of structure is the fact that many of the cerebral arteries are "straight arteries," that is their axis is in a direct line of the blood stream, and on that account they are particularly subjected not only to the highest mean blood pressure, but also to the direct blow of the cardiac systole. As is well known these same arteries are prone to the lodgment of bacterial emboli, which are among the unquestionable excitors in many instances of arteriosclerosis. Dana and others have shown that in some conditions cerebral atrophy, by a lowering of the external or supporting pressure on the cerebral arteries favors over-distension and the origin of inflammatory processes. Still other inductive factors are at work, such as for example the great physiological activity of these trunks, but the chief points have already been stated.

The causes of arteriosclerosis of the central nervous system do not differ from those producing the lesions in the general arterial tree, and we may primarily classify them under physiological and pathological.

Physiological arteriosclerosis is a normal process in old age. The anatomical changes characteristic of senile or physiological arteriosclerosis do not differ materially from the changes seen in the pathological condition. Minor differences in the location and extent of the lesion and in certain special and inconsequential characteristics, exist in some instances but generally to only a negligible degree. In old age the condition is found as among the early signs of malnutrition and beginning tissue death.

Pathological arteriosclerosis may be broadly and yet not inaccurately defined as premature or abnormally induced arterial senility. The etiological factors may be best considered under the headings of mechanical, infectious and toxic. In many cases all are concerned, and in most, more than a single agent must be considered. Some observers also cite heredity as one of the determining agents, and doubtless the disease is hereditary in some instances, but only where the transmission of formation of certain toxic substances takes place or where exposure to certain conditions predisposing to the disease exists in families from generation to generation. We must admit, however, on theoretical grounds, the possibility of purely fetal characteristics which may predispose, as in maldevelopment of the vascular system, or some inherent flaw, such as for instance probably exists in hemophilia.

Under the mechanical factors must be considered all those conditions which induce abnormally high blood pressure, such as physical overwork, particularly exemplified in improperly trained athletes, or where from any reason the blood pressure is relatively raised, as for example in caisson workers. It is notable that it is much more commonly caused where the blood pressure is raised to a high point sporadically, as in athletic contests, and relatively less often where the pressure is habitually raised, as in laborers.

Infectious agents usually act through the formation of bacterial emboli or thrombi, from which infection of the vessel walls extends. External infections through the adventitia may also occur in cases, as where a vessel passes through an inflammatory area. Stengel states that periarteritis nodosa is usually caused in this manner, though also admitting that it may at times have a definite special pathology.

Toxins are doubtless the more common and important etiological factors concerned in arteriosclerosis. Certain of the toxemias are of infectious origin, as for instance in diphtheria or chronic tuberculosis. In other instances the poisons may be autogenous, as in habitual constipation, over-alimentation, or in malnutrition of various types. The more common toxic conditions are those occuring in alcoholism, chronic nephritis, lead poisoning, gout and rheumatism. In nearly all these conditions it is practically certain that the causative factor is not a simple one, but that in each case it is complicated by other secondary agents; thus excessive blood pressure takes place in nephritis, and in nearly all the conditions, intestinal toxemias, malnutrition and other subsidiary factors are present.

Syphilis is one of the most common disease conditions producing arteriosclerosis in its most exquisite types. Arteriosclerosis is almost invariably present in syphilis, and cases of this contagion in which arterial disease never develops, are the exception. Syphilitic arteriosclerosis is particularly prone to attack the vessels of the central nervous system. The reasons for this generally admitted fact are various; probably the most logical of them is the idea propounded, we believe by Dana, namely, that the syphilitic poison acts especially on the cerebral arteries, since they are literally bathed on both sides by the blood and toxic lymph circulating in the perivascular lymph spaces.

Numerous types of arteriosclerosis are differentiated by various authors, and unfortunately hardly any two agree absolutely on even the simple definition of arteriosclerosis. The disease is sometimes classified, according as it is chiefly manifested by alterations in the intima, media or adventitia, but this is very unsatisfactory, since one rarely or never finds a case in which all the arteries of one body or even viscus are changed in precisely the same manner. It is also rare to find an artery in any except the acute stages in which the process is limited solely to any one coat; hence it is that these finer classifications are inaccurate anatomically, and it is well for us to realize that except for acute or specific types of arteriosclerosis, such as septic or tubercular, the condition is a general one differing only in degree or in the type of the secondary, i.e., degenerative alterations, which follow the primary inflammatory manifestations.

Some authors classify arteriosclerosis anatomically according to the cause of its development; they thus speak of alcoholic arteriosclerosis, syphilitic arteriosclerosis, and so on. Now as a matter of anatomical fact, these distinctions do not exist. Syphilitic arteriosclerosis, the type most minutely differentiated, usually does not differ anatomically from many other forms which may be caused by other factors, except where the walls of the artery are actually the seat of a gummatous or syphilitic process. With this statement we must, however, admit that certain forms are more frequent where syphilis is present than in non-syphilitic cases, thus periarteritis is more common in lues, probably for the reasons already cited, and fatty degeneration is also more often seen than is calcareous infiltration of the arterial walls.

It remains then for us to classify the various forms of arteriosclerosis as acute or chronic, remembering that these merge one into the other with no distinct line of demarcation. The condition may also be quite correctly classified according to the type of alteration or degeneration predominating in the diseased trunks.

Concerning the manner of development of the changes in arteriosclerosis much experimentation and many observations have been made so that now, though many points still remain unknown the more common methods of formation are fairly well demonstrated, particularly by the work of Gall and Sutton, of Thoma, Koster and others. The older pathologists thought that as a rule the fibrous hyperplasia, which is characteristic in greater or less degree of all forms of the disease, was immediately excited by the direct irritation produced by some abnormal substance circulating in the blood, so acting on the intima primarily and secondarily perhaps on the remaining arterial walls. Of course, where the arteries are surrounded by an inflammatory area, as when they pass through an abscess, direct extension from the adventitia is admitted.

Although this theory no longer holds first place in the minds of most students, it is certainly one of the methods, as has been amply demonstrated by experiments. Undoubtedly the chief condition underlying the development of the disease lies in any state which decreases the elasticity of the arterial wall, whether permitting it to over-distend or preventing its physiological contraction. This may be brought about by many different changes in the walls of the artery. In those cases in which the disease seems to be inaugurated as a result of excessive blood pressure, it is probably brought about by over-distension, resulting in injury of the fenestrated layers and possibly of the muscle coat, with the result that the lumen of the artery remains more or less permanently distended. Probably as an effort on the part of nature to restore the normal caliber of the tube, and, at the same time, to strengthen the weakened and dilated walls, hyperplasia of the areolar connective tissues takes place. Only the white fibrous elements take part in this hyperplasia; the yellow elastic fibers do not hypertrophy, whereas in physiological thickening of the arterial wall such as takes place in the arteries of well trained athletes or in the vessels of laborers hyperplasia of this coat does eventuate.

In certain cases this hyperplasia, which may be compared to like processes taking place in numerous similar conditions in other parts of the body, becomes so marked as to limit the lumen of the artery to a greater or less extent. At the same time the strength of the wall is decreased rather than increased, not only on account of the lack of elasticity of the tissue formed, but also since it is of low grade and is very likely to undergo various types of degeneration, notably fatty and calcareous. Degeneration takes place whether blood vessels are formed in the new tissue or not, though sometimes trunks springing from the vasa vasorum are very numerous and extend into the innermost coat of the intima.

This sequence of affairs is induced not only when the integrity of the arterial wall has been impaired by increased blood pressure or direct traumatism, but also when, through any cause whatsoever, the physiological activities of the arterial walls are obtunded. It therefore occasionally occurs as the result of trophic faults following disease of the nerve fibrils which normally control the media or muscle coat. One frequently finds extreme examples of this variety in the vessels supplied to paralyzed extremities. It is stated that in such instances the interstitial changes are most pronounced in the media coats, but unless seen in the early stages this is difficult to demonstrate, since it very soon also extends to the other walls of the artery, which may have become diseased as a secondary process, following the incompetence of the muscle coat.

Probably the most frequent factor back of these arterial changes lies in conditions which impair the nutrition of the arterial walls. One of the most frequent of these is a diseased condition of the vasa vasorum, on which the arterial walls are immediately dependent for their nourishment. If the caliber of these minute vessels becomes obliterated or limited by any process, such as arteritis or thrombosis, the portions of the arterial walls depending on these particular vessels for their nourishment lose their elasticity, the power of contraction or relaxation, and the vessel at this point distends under the blood pressure, and the hyperplastic alterations mentioned become set up as an attempt at compensation.

Another type of arterial disease depending for its origin on the vasa vasorum is seen in those cases of arteriosclerosis where the nutrient arteries are surrounded by exudates of small round cells. Arteriosclerosis is undoubtedly inaugurated in this manner by a primary arteritis of the vasa vasorum accompanied by cellular exudate from which the process becomes diffused. The "periarteritis simplex" described by Charcot, which occurs frequently in the cerebral arteries and leads to the formation of miliary aneurisms, is probably of this manner of formation. The disease is then primarily in the adventitia, but subsequently spreads to the other coats, the degeneration of which produces the deficient areas which subsequently become dilated into aneurisms of more or less size.

Another disease condition probably sometimes inducing arteriosclerosis through the weakening of the arterial wall, is where some type of primary degeneration, as hyaline or albuminoid, invades the coats which then dilate and is followed by interstitial hyperplasia. It is more probable, however, that the interstitial hyperplasia is generally succeeded rather than preceded by such forms of degeneration.

It is foreign to the subject of this paper to attempt a decription of the various anatomical varieties of arteriosclerosis, and at best this is a thankless task since the varieties described are so numerous. All can however be included under the headings of the various types of degeneration following acute, subacute and chronic inflammatory disease affecting the walls of the arteries. As already stated the type of the degenerative change is not usually found to be the same throughout the entire body, and the various classifications are more properly considered as stages in the same process than as different forms of a disease.

SYPHILIS OF CEREBRO-SPINAL AXIS.

Showing marked arteriosclerosis of the blood vessels of the spinal cord.

J. R., Montefiore Hospital. Aged fifty-three years. Widower. Occupation, manager. Family history negative.

Previous History.—Usual diseases of childhood. Has had gonorrhea "very often." Had a sore on penis 30 years ago, indurated and accompanied by enlargement of inguinal glands. Rash all over body followed, loss of hair of head and eyebrows. Was treated for syphilis for six months, symptoms all disappeared. Thinks that he had another hard chancre 27 years ago. Has had chancroids frequently, has had epididymitis and usual complications of gonorrhea. Patient states that he has had "Every disease that a lady can give a man." Has used alcohol and tobacco to excess. Masturbated as a young man, has constantly indulged in sexual excesses. Wife has had two miscarriages, both at about third month, no living children.

Present illness.—Twenty-two years ago had pains in toes with sensations of constriction in calves, finally typical girdle pains. Fell in street while running after a car, has not been able to run since, but could walk when assisted. One year later became cross-eyed and had diplopia. Became impotent. Lost control of bladder. Had respiratory crises, unsteadiness of hands, etc. Symptoms have increased up to present day.

Present complaints.—Excruciating boring pains all over. Inability to walk. Incontinence of urine. Ataxia in hands.

Physical examination.—Extreme ataxia in legs. Lower extremities very flaccid. Marked Romberg. Pupils do not react to light, not consensually, ocular movements impaired, convergent strabismus, nystagmus. No atrophies of upper extremities, though muscles are very flaccid, contractions, slow and vermiform. Reflexes present on both sides, but markedly ataxic. Knee-jerks, Achilles and plantar reflexes absent. Interscapular, epigastric, abdominal and cremasteric reflexes absent. Marked slowness of muscular contractions throughout. Abdomen and lower extremities anesthetic.

Examination of heart, lungs, liver, spleen and kidneys show nothing of especial note.

Appears to be mentally sound.

Present history.—After remaining in the hospital several years, showing very little improvement under the usual methods of treatment, patient suddenly died with the symptoms of pulmonary embolism.

Post-mortem examination showed: (Abstract of protocol.)

Heart.—Fatty degeneration and brown atrophy. Marked sclerosis of coronaries. Chronic endocarditis of aortic and mitral segments.

Aorta.—Marked endarteritis with extensive areas of fatty degeneration and occasional patches of calcification. Same present in large trunks of thorax and neck. Areas of necrotic softening in walls of arteries.

Lungs.—Thrombosis of both pulmonary arteries. Chronic pneumonia. Chronic bronchitis.

Liver.—Fatty degeneration with lobular cirrhosis.

Stomach and intestines.—Chronic congestion.

Spleen and lymph nodes.—Generally enlarged, hyperplastic lymph-adenitis.

Kidneys.—Numerous old infarctions. Chronic interstitial nephritis.

Brain.—Examination not permitted.

Spinal cord and medulla.—Irregular areas of both ascending and descending degeneration. Marked arteriosclerosis. (All findings verified microscopically.)

EXAMINATION OF ARTERIES OF SPINAL CORD.

Medium sized vessels.—The perivascular connective tissue throughout shows a moderate degree of thickening and a good many of the connective tissue cells in this distribution are filled with pigment. This change is also continued into the adventitia, but it is not very pronounced and no fibroblasts are found, the change being apparently a chronic one. The media coat shows very slight alteration in the vessels of this caliber. The muscle fibers are distinct, but are not separated by an abnormally abundant interstitium nor do these cells show any evidences of degeneration except in a few instances where slight hyaline changes are to be made out.

The internal fenestrated membrane is well developed in the greater number of the medium sized arteries, but is not abnormally thickened.

The intima coat is greatly increased, the thickness varies considerably, but in places equal three or four times that of the remainings walls of the corresponding vessels, though for the greater part the increase is not greater than two to three times the thickness of the normal intima. Fibroblasts and proliferating connecting tissue cells are abundantly present in this coat, so much so that in places the structure closely resembles that of embryonic connective tissue. Areas of fatty and atheromatous degeneration and ocasional small patches of round-celled infiltration are frequent. Hyaline degeneration is very pronounced in this coat in some of the arteries, while others are nearly free from it. Calcification is not present in any of the vessels of this class.

The endothelial coat is mostly intact, though over some of the more marked areas of thickening the cells show evidences of reproduction and are occasionally desquamated.

The vasa vasorum show very slight alterations and none which are constant.

As a rule the medium sized arteries are but moderately filled with blood.

Small sized arteries.—The supporting tissue of the small sized arteries and arterioles is perhaps slightly increased, but, it shows as its most marked characteristic hyaline degeneration extending out from the walls of the more extensively diseased arteries. The adventitia shows the same characteristics as the supporting tissue, but in the greater number of places remains practically normal.

The media and intima in most of the arterioles is fused into a single layer with a thickness about double that normal to these layers. The entire mass of the tissue shows a diffuse hyaline degeneration of very pronounced degree. Occasionally abnormal hyperplastic connective tissue cells can be made out, but as a general thing all structure except for an indistinct fibrillar mesh is obliterated.

The endothelium of the intima shows occasional large atypical cells, characterized by very large nuclei, irregular shape and small quantity of widely separated chromatin.

Many of the smaller vessels are enclosed in an abnormally dilated perivascular lymph space which is occasionally filled by granular detritus. Corpora amylacea are frequent about some of the vessels, but they appear to bear a more direct relationship to the connective tissue stroma than to the vessels as such.

Capillaries.—Unlike the arteries, the capillaries are, for the greater part, well filled with blood cells. A good many of them are surrounded by neuroglia which is perceptibly increased in density. Some of them show a partial blocking of the lumen with large atypical endothelial cells.

ARTERIOSCLEROSIS OF THE BRAIN AND SPINAL CORD, OCCURRING IN ALCOHOLISM.

J. M., male, aged forty-two years. Wd. 32 Bellevue Hospital.

Patient entered hospital in semiconscious state and not able to give a coherent history. Friends state that he has been a heavy drinker of whiskey and beer for years. He had delirium tremens several times. He has used alcohol constantly, but of late has been drinking more than ordinarily.

The physical examination and clinical course of the disease present the usual picture of delirium tremens, and patient died after four days in hospital.

Abstract of protocol. Verified by microscopical examination.

Heart.—Interstitial myocarditis, brown atrophy and fatty degeneration. Marked sclerosis of coronary arteries.

Lungs.—Chronic miliary tuberculosis of apices. Chronic congestion, emphysema and anthracosis.

Liver.—Fatty degeneration. Chronic congestion. Moderate interstitial hepatitis.

Spleen.—Chronic congestion with marked pigmentation. Periarteritis of smaller arteries.

Pancreas.—Chronic congestion. Parenchymatous degeneration.

Kidneys.—Marked parenchymatous with fatty degeneration. Acute congestion of blood vessels. Extensive epithelial desquamation. Moderate interstitial increase.

Stomach.—Chronic gastritis. Recent hemorrhages into mucosa.

Adrenals.—Extreme congestion with minute medullary hemorrhages. Fatty degeneration of parenchymatous cells.

Cerebrum.—Marked edema of pia-arachnoid. Old areas of meningeal thickening. Moderate cerebral edema and congestion, brain otherwise macroscopically normal. Microscopically a good many degenerated fibers are found in the subcortical layer of the Rolandic adeas. Certain ganglion cells of the corresponding gray matter show chromatolysis and atrophy.

Spinal cord.—Macroscopically normal. Microscopically a good many degenerated fibers are found, particularly in the direct and crossed pyramidal tracts and in the anterior radicular zone. There is a general increase in the connective tissue framework of the cord, and corpora amylacea are frequent in the interstitium adjoining the adventitia of many of the vessels.

Special examination of the blood vessels of the brain and cord.—There is a general dilatation of the perivascular lymph spaces in both the cord and cerebral tissues. Both small and medium sized arteries are similarly affected, but the dilatation is more marked about the smaller trunks. The supporting connective tissue of the arteries is generally increased, the spinal arteries showing this change in more marked degree than the cerebral vessels. The adventitia of most of the medium sized arteries is thickened in moderate degree; this is more apparent in the spinal vessels than in the cerebral. Very few hyperplastic connective tissue cells, that is fibroblasts, are demonstrable in this coat, but the process seems to have been a chronic productive one.

The media shows a production of connective tissue between the muscle cells, causing pressure atrophy, so that the coat is mostly replaced by fibrous connective tissue of the adult type. The disease of this layer is probably largely responsible for the abnormal distension of most of the vessels. The hyperplastic connective tissue is almost entirely of the areolar type and there appears to be little if any increase in the yellow elastic fibrils.

The subendothelial layer of the intima shows a more pronounced, though very irregular hyperplasia, and in this coat a few fibroblasts appear. Small patches of round cell infiltration are present, and in a few places where the thickening of the coat has been most pronounced, it is sufficient to cause bulging into the lumen, with disintegration and athermomatous degeneration of the hyperplastic tissue. As a rule little change is to be seen in the endothelial layer of the vessels of medium size, but a few of the cells show swelling. The endothelium of the vasa vasorum is seen to be considerably swollen in many places and many of the vessels are occluded with a clot, a part of which is of the white variety. Very little absolute alteration, aside from that mentioned, can be made out in the walls of these very minute vessels, but a considerable number of them seem to be compressed by the hyperplastic connective tissue of the walls of the artery at large; hence the circulation in them has probably been impeded.

The small arteries show the increase in the adventitia to a lesser degree than those just described, but the media shows a very scant supply of muscle cells, and is largely replaced by the hyperplastic tissue; in addition there is a diffuse hyaline degeneration of the coat in many of the vessels. This change also extends into the subendothelial coat and involves the fibroblasts which are found quite abundantly in the smaller trunks. Swelling, and in places desquamation of the endothelium, is present, particularly over those parts where the degeneration of the subendothelial coat is most extensive.

Many of these smaller trunks are filled by clot, a considerable portion of which is of the white variety, but as a rule their lumen is distended and filled with blood.

The capillaries are mostly congested with blood. The lymph space about them is generally dilated, and in a few cases rupture of the capillary wall has permitted the extravasation of a few cells. In some cases the endothelium of the capillaries seems to be in a state of karyokinesis. A good many capillaries are plugged by clot.

ACUTE ARTERITIS OCCURRING IN THE VESSELS OF THE CENTRAL NERVOUS SYSTEM IN RABIES.

J. B., aged thirty-two years. Machinist. Admitted to Hood Wright Hospital April 16, 1902, 9.20 p.m.

Family history.—Unimportant.

Past history.—Two months ago (February 15 or 16) patient was bitten by a small fox terrier, which gave no sign of being rabid. The bite took place in the fleshy part of the right thumb. The patient sucked the wounds as soon as the dog let go but paid no further attention to them; they healed within a week.

Present history.—April 15 patient noticed an itching or pinching sensation in the right hand about the old wounds and felt chilly. April 16 he complained of some pain in the hand and shoulder of the same side and began to have some difficulty in swallowing liquids.

Examination.—Perfectly conscious, rational, and shows no excitement. No paralysis. Sensation of numbness in right hand and fingers. Heart, lungs, liver, spleen and kidneys, negative. T, 99.6; P., 72; R., 24. Patient drinks with great difficulty and only after considerable exertion.

The patient finally developed the typical symptoms of rabies, failed to respond to the most energetic treatment and died April 18, two days after admission. In the latter stages of the disease he showed marked hypersecretion of saliva, and the temperature rose to 104.2 degrees. The pulse became very rapid and feeble and blood count showed a leucocytosis of 26,000.

Post-mortem examination showed in brief very few gross changes aside from a slight arteriosclerosis of the general vessels, acute lymphangitis and pulmonary edema.

Microscopic examination demonstrated very few changes in brain and cord except chromatic alterations in the ganglion cells, particularly those of the medulla, and the alterations of acute lymphadenitis. The blood vessels of the central nervous system show the marked changes of acute arteritis to be described in detail.

Experimental inoculation of rabbits with emulsions of the medulla and cord caused the development of rabies in these animals. The case was thus demonstrated to be a typical one of rabies.

The changes noted in the arteries are most marked in the medulla, though they are also present, but in considerably less degree, in the vessels of other portions of the brain and cord. A good many of the arteries show absolutely no change whatsoever. The medium sized vessels are but slightly involved, the chief changes being found in and about the small arteries and arterioles. The perivascular lymph space is markedly dilated in almost every instance. The connective tissue cells of the supporting tissue, of the scant adventitia and of the intima show, almost without exception, frequent evidences of active cell division, and the endotheloid cells seen in the perivascular lymph spaces also exhibit frequent karyokinetic figures. There is a very marked exudation of leucocytes, chiefly small mononuclears, into the walls of the vessels, where they separate the fibers and muscle tissue and infiltrate into the lymph spaces, where they mingle with desquamated fibroblasts and proliferating endothelial cells. The endothelium of the intima also shows evidences of active cell division. Polynuclear leucocytes are found about the periphery of the channels, where they are united to the eroded endothelial wall by shreds of fibrin. Notwithstanding the fact that the walls of many of the vessels are seriously damaged, diapedesis of the erythrocytes is not shown. There is a slight mesh work of fibrin present throughout the vessel walls.

Changes of like character, but of less extent, are also found about the capillaries but, as is the case with the arteries, they are not universally involved.